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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/981,239	10/18/2001	Rita De Santis	2818-64	6035

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EXAMINER	
QIAN, CELINE X	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 01/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/981,239	DE SANTIS, RITA	
	Examiner	Art Unit	
	Celine X Qian	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *50-65* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *50-65* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 October 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 50-65 are pending in the application.

This Office Action is in response to the Amendment filed on 10/28/03.

Response to Amendment

The rejection of claim 39 under 35 U.S.C. 112 2nd paragraph is moot in light of Applicant's cancellation of the claims.

The rejection of claims 32-35, 39, 42, and 47-49 under 35 U.S.C.102 is moot in light of Applicant's cancellation of the claims.

The rejection of claims 40, 41, 43 and 46 under 35 U.S.C.103 (a) is moot in light of Applicant's cancellation of the claims.

Claims 50-65 are rejected under 35 U.S.C. 112 1st paragraph for reasons discussed below.

Claims 50-65 are rejected under 35 U.S.C. 112 2nd paragraph for reasons discussed below.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 50-65 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: (a) the nature of the invention; (b) the breadth of the claims; (c) the state of the prior art; (d) the amount of direction provided by the inventor; (e) the existence of working examples; (f) the relative skill of those in the art; (g) whether the quantity of experimentation needed to make or use the invention based on the content of the disclosure is "undue"; and (h) the level of predictability in the art (MPEP 2164.01 (a)).

The nature of the invention

The claims are drawn to a method for the generation of cells presenting cancer-testis antigens (CTA) comprising: a) collecting peripheral blood mononuclear cells from a subject; b) activating said collected cells to form activated cells; c) culturing and optionally expanding *ex vivo* said activated cells; d) treat said cultured cells four times every 12 hours; then replacing half of the culture with fresh medium and allowing to proceed for additional 48 hours so that said cells express said antigen. The specification teaches that the cells obtained from this process will be utilized as autologous cellular vaccines to immunize cancer patients against CTA potentially expressed on their own tumor tissues.

The state of art and the level of predictability in the art

The state of art at the time of filing considers the clinical success of cancer vaccines as unpredictable. The applicants' attention is directed to the teachings of Bodey et al. (Anticancer Res 2000;20:2665-76), and Radoja et al. (Mol Med 2000;6:465-79), which teaches the potentials and limitations of various forms of cancer vaccines and immunotherapy. Rodoja et al. review

the mechanisms of tumor cells evades host immunity. Such mechanisms include: secretion of suppressive factors in the tumor microenvironment, the lack of expression of costimulatory signals on tumor cells, induction of regulatory T cells having a suppressive phenotype, loss of antigen presentation function in tumors, tumor-induced T cell signaling defects, loss of tumor antigen expression and immuno-tolerance (see page 466, 1st col., 1st paragraph). Bodey et al. teach that the cancer vaccine approach to therapy is based on the notion that the immune system could possibly mount a rejection strength response against the neoplastically transformed cell conglomerate (see abstract). However, Bodey et al. indicate that due the problems as discussed by Rodoja, the expectation of utilizing host immune system against tumor cells is rarely fulfilled. Bodey et al. further discussed the potential of using tumor associated antigen (TAA) for designing cancer vaccine (see page 2668 2nd col., 2nd paragraph). Despite several decades of clinical and basic research, Bodey et al. indicates that active specific immunotherapy for cancer vaccine is still in its scientific infancy. In trials for using cells expressing TAA as potential cancer vaccines, another obstacle is the development of significant cytotoxic cellular immune responses following allogeneic vaccination. Although cancer vaccine approach to immunotherapy has been shown in most cases to result in an *in vitro* or s.c. enhancement of TAA targeted immunity, the malignant tumor does in most cases progress and overwhelm the host even after considerable remission. Bodey et al. point out this apparent contradiction is the defining characteristic of the difficulties associated with an immunologic approach to generation of cancer vaccines.

The teaching of the specification

The teaching of the specification is limited. Although the specification teaches how to make cells expressing CTA, it fails to teach how to use such cells as cellular vaccine for cancer patients. The specification fails to provide any support for the enablement of using the cells expressing CTA as cancer vaccine because the specification does not provide any teaching to overcome the art recognized unpredictability for generating cancer vaccines that have therapeutic effects. As such, one of skilled in the art would have to engage in undue experimentation to use these cells. Therefore, the claimed invention is not enabled.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 50-65 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claims 50-65, the word "derived" renders the claim indefinite because the nature and number of derivative process is unknown. As such, the metes and bounds of the claim cannot be established.

Regarding claim 59, the recitation of "wherein histone deacetylase inhibitors are further used in step d)" renders the claim indefinite because it is unclear how such histone deacetylase inhibitors are used. It is unclear whether said inhibitor is used before, during or after pulsing with hypomethylating agents.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 61 is rejected under 35 U.S.C. 102(b) as being anticipated by Shichijo et al.

Claim 61 is a product by process claim, which read on the product, cells that express cancer-testis antigens. Shichijo et al. disclose cells expressing MAGE (see Table 1). Therefore, Shichijo et al. disclose the instantly claimed invention.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X Qian whose telephone number is 703-306-0283. The examiner can normally be reached on 9:00-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel Ph.D. can be reached on 703-305-1998. The fax phone number for the organization where this application or proceeding is assigned is 703-305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Celine Qian, Ph.D.

Anne-Marie Falk

ANNE-MARIE FALK, PH.D
PRIMARY EXAMINER